IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	David J. Grainger et al.	Examiner: Theodore Criares
Serial No.:	09/754,775	Group Art Unit: 1617
Filed:	January 4, 2001	Docket: 295.009US3
Title:	PREVENTION AND TREATMENT OF CARDIOVASCULAR PATHOLOGIES WITH TAMOXIFEN ANALOGUES	

RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Restriction Requirement mailed July 3, 2002, Applicant provisionally elects, with traverse, the claims of Group II (claims 173-211), directed to a therapeutic method for preventing or treating a cardiovascular or vascular indication characterized by a decreased lumen diameter, which includes administering to a mammal at risk of or afflicted with said cardiovascular or vascular indication a cytostatic dose of a compound of formula (I); a therapeutic method of increasing the level of TGF-beta in a mammal in need thereof, which includes administering an effective amount of a compound of formula (I); a method of increasing the level of TGF-beta in a mammal in need thereof, which includes administering an effective amount of an agent that directly or indirectly elevates the level of active TGF-beta in said mammal, wherein the agent has reduced estrogenic activity relative to tamoxifen, reduced DNA adduct formation relative to tamoxifen, or any combination thereof; and a therapeutic method for preventing or treating a vascular indication characterized by a decreased lumen diameter, which includes administering to a mammal at risk of or afflicted with said vascular indication, a cytostatic dose of a compound of formula (I). Reconsideration and withdrawal of the Restriction Requirement, in view of the remarks herein, is respectfully requested.

In the Restriction Requirement, the Examiner groups the following claims together: Group I includes claims 158-172 and 225-231 (drawn to a therapeutic method comprising inhibiting non-aortal vascular smooth muscle cell proliferation associated with procedural vascular trauma); Group II includes claims 173-181, 207-211 and 232 (drawn to a therapeutic method for preventing or treating a cardiovascular or vascular indication characterized by a decreased lumen diameter); Group III includes claim 232 (drawn to a method of treating diabetic retinopathy); and Group IV includes claims 212-230 (drawn to a therapeutic stent). However, based on the

Examiner's characterization of the groups, it is respectfully submitted that the claims in Group I are claims 158-172 and 225-231, the claims in Group II are claims 173-181 and 207-211, the claim in Group III is claim 232, and the claims in Group IV are claims 212-224. The Examiner also indicated that claims 182-206 would be examined if any of Groups I-IV were elected.

The Restriction Requirement is traversed on the basis that the inventions are so closely related that they cannot be properly considered independent and distinct within the statutory meaning of 35 U.S.C. § 121. In particular, claims directed to a therapeutic method for preventing or treating a cardiovascular or vascular indication characterized by a decreased lumen diameter, which includes administering to a mammal at risk of or afflicted with said cardiovascular or vascular indication, a cytostatic dose of compound of formula (I); a therapeutic method of increasing the level of TGF-beta in a mammal in need thereof, which includes administering an effective amount of a compound of formula (I); a method of increasing the level of TGF-beta in a mammal in need thereof, which includes administering an effective amount of an agent that directly or indirectly elevates the level of active TGF-beta in said mammal, wherein the agent has reduced estrogenic activity relative to tamoxifen, reduced DNA adduct formation relative to tamoxifen, or any combination thereof; and a therapeutic method for preventing or treating a vascular indication characterized by a decreased lumen diameter, which includes administering to a mammal at risk of or afflicted with said vascular indication, a cytostatic dose of a compound of formula (I) (claims 173-211; Group II) are clearly related to at least claims directed to a therapeutic method comprising inhibiting non-aortal vascular smooth muscle cell proliferation associated with procedural vascular trauma, which includes administering to a mammal, such as a human, subjected to said procedural vascular trauma an effective cytostatic antiproliferative amount of a compound of formula (I), a therapeutic method comprising inhibiting vascular smooth muscle cell proliferation, which includes administering to a mammal an effective cytostatic antiproliferative amount of a compound of formula (I), and a therapeutic method for treating a condition selected from the group consisting of arteriosclerosis and small vessel disease, which includes administering to a mammal afflicted with said condition, an effective amount of a compound of formula (I) (claims 158-172 and 225-231; Group I), and claims directed to a method of treating diabetic retinopathy by increasing the level of TGF-beta in a mammal in need

thereof, which includes administering an effective amount of a compound of formula (I) (claim 232; Group III). Thus, the claims in Groups I-III are directed to methods of using an agent such as a compound of formula (I), e.g., wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H, R^5 is I, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H or together with R^3 is -CH_2-CH_2- or -S-, R^5 is I, OH, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H; or an agent that elevates the level of active TGF-beta.

The Restriction Requirement is also traversed on the basis that Restriction Requirements are optional in all cases. If the search and examination of an entire application can be made without a serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions. M.P.E.P. § 803. For example, the claims of at least Groups I and II can be efficiently and effectively searched in a single search as these claims fall within the same class (class 514) for search purposes.

Therefore, the Restriction Requirement is properly traversed, and reconsideration is requested.

The Examiner is invited to contact Applicant's Representatives at the number given below if there are any questions regarding this Response or if prosecution of this application may be assisted thereby.

Respectfully submitted,

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Date September 3, 2002 By

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 3rd day of September, 2002.

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